Immunogenicity of induced pluripotent stem cells.

Journal: Nature

Publication Year: 2011

Authors: T Zhao, Z N Zhang, Z Rong, Y Xu

PubMed link: 21572395

Funding Grants: Developing induced pluripotent stem cells into human therapeutics and disease models

Public Summary:
Taking advantage of the inbred mouse strain that has identical genetic background, we produce integration-free mouse iPSCs that can be transplanted back into genetically identical mice. In contrast to the popular belief, our findings indicate that cells differentiated from mouse iPSCs are immunogenic in the genetically identical mice. We further show that this immunogenicity is due to the abnormal expression of immunogenic proteins during the differentiation of iPSCs, possibly as a result of the abnormal DNA methylation of the genome of iPSCs. In summary, the immunogenicity of therapeutically valuable cells derived from patient-specific iPSCs should be evaluated before any clinic application of these autologous cells into the patients

Scientific Abstract:
Induced pluripotent stem cells (iPSCs), reprogrammed from somatic cells with defined factors, hold great promise for regenerative medicine as the renewable source of autologous cells. Whereas it has been generally assumed that these autologous cells should be immune-tolerated by the recipient from whom the iPSCs are derived, their immunogenicity has not been vigorously examined. We show here that, whereas embryonic stem cells (ESCs) derived from inbred C57BL/6 (B6) mice can efficiently form teratomas in B6 mice without any evident immune rejection, the allogeneic ESCs from 129/SvJ mice fail to form teratomas in B6 mice due to rapid rejection by recipients. B6 mouse embryonic fibroblasts (MEFs) were reprogrammed into iPSCs by either retroviral approach (ViPSCs) or a novel episomal approach (EiPSCs) that causes no genomic integration. In contrast to B6 ESCs, teratomas formed by B6 ViPSCs were mostly immune-rejected by B6 recipients. In addition, the majority of teratomas formed by B6 EiPSCs were immunogenic in B6 mice with T cell infiltration, and apparent tissue damage and regression were observed in a small fraction of teratomas. Global gene expression analysis of teratomas formed by B6 ESCs and EiPSCs revealed a number of genes frequently overexpressed in teratomas derived from EiPSCs, and several such gene products were shown to contribute directly to the immunogenicity of the B6 EiPSC-derived cells in B6 mice. These findings indicate that, in contrast to derivatives of ESCs, abnormal gene expression in some cells differentiated from iPSCs can induce T-cell-dependent immune response in syngeneic recipients. Therefore, the immunogenicity of therapeutically valuable cells derived from patient-specific iPSCs should be evaluated before any clinic application of these autologous cells into the patients.